

U.S.S.N. 10/044,538

Filed: January 10, 2002

**AMENDMENT AND RESPONSE AFTER FINAL****Remarks**

Claims 1-26 are pending. Claims 1-3, 6-18, 20, 21, 23, 24, 25, and 26 have been amended. Claims 1-3, 6-18, 20, and 23-24 have been amended to correct grammatical errors. Claims 3, 21, 25, and 26 have been amended to correct antecedent basis.

**Rejection Under 35 U.S.C. § 112, second paragraph**

Claims 4, 12 and 25 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to define the metes and bounds of the invention. Applicants respectfully traverse this rejection.

Definiteness of claim language must be analyzed, not in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary skill in the pertinent art at the time the invention was made. The test for definiteness under 35 U.S.C. 112, second paragraph is whether those skilled in the art would understand what is claimed when the claim is read in light of the specification. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 U.S.P.Q. 2d 1081, 1088 (Fed. Cir. 1986). "If the scope of the subject matter embraced by the claims is clear, and if the applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. § 112, second paragraph" (MPEP 2173.04).

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Claim 4 recites a biodegradable polycation compound according to claim 1, wherein the polysaccharide chain is selected from the group consisting of dextrans, arabinogalactan, pullulan, cellulose, cellobios, inulin, chitosan, alginates and hyaluronic acid, wherein the polysaccharide chain contains an amount of saccharide ranging from 2 to 2000 saccharide units.

A claim to a chemical compound is not indefinite merely because a structure is not presented or because a partial structure is presented. The courts have consistently maintained that chemical compounds may be claimed by a name that adequately describes the material to one skilled in the art. *Martin v. Johnson*, 454 F.2d 746, 172 U.S.P.Q. 391 (CCPA 1972).

One of ordinary skill in the art knows the meaning of the term alginates and dextrans. For example, the USPTO's U.S. Manual for Classification defines *dextran or derivative* as higher molecular weight polysaccharides containing D-glucose units linked predominantly by C-1 → C-6 glycosidic bonds. Dextrans or derivatives yield glucose upon hydrolysis but differ from starch and glycogen in terms of their molecular structure (Class 524, Subclass 54). The relevant sections of the manual are enclosed. Alginates are salts of alginic acid, which is a polyuronide made of a sequence of two hexuronic acid residues: (beta)-D-mannuronic acid and (alpha)-L-guluronic acid. The two monosaccharides are not distributed at random, but rather form blocks of up to 20 units.

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The number and length of the blocks are important factors in determining the physical properties of the polymer. Several references defining alginates are enclosed.

Polysaccharides are defined as linear, branched or crosslinked natural or *chemically modified* polysaccharides (page 14, lines 10-14). The polysaccharide carrier is selected in order to enhance the degree and efficiency of transfection (page 14, lines 20-21). For example, polymers can be selected based upon the density and distribution of the cationic sites on the polymer to obtain transfection agents that are tailored to the anionic charge distribution of the nucleic acid being transfected (page 14, lines 22-24). Various substituents can be incorporated into the polymer carrier in order to improve the transfection efficiency. For example, hydroxyl groups on the aliphatic chain of the monosaccharide can be substituted with aliphatic hydrocarbons, amides, azo, carbamate, carboxylic esters, ethers, thioethers, thiols, fluorescent derivatives and sulfonic acids (page 15, lines 26-30). Further, the hydrophobicity or hydrophilicity of the polymer can be increased by alkylating the secondary amines with long chain hydrocarbons or polyethylene glycol, respectively. The structure of the polymer can also be altered, by known techniques, to optimize the transfection and delivery of the polymer for each cellular target on the basis of the physiological and biological characteristics of that target. For example, protein ligands can be covalently coupled to the polymer and then incorporated into the ligand-nucleic acid complex (page 16, lines 3-11).

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As evidenced by the printouts submitted with this response, one of ordinary skill in the art would understand, in view of the applicant's disclosure, that the terms **alginates** and **dextrans** includes alginates and dextrans which have been *chemically modified* (i.e. derivatives), in order to enhance the degree and efficiency of transfection. Accordingly, claim 4 is not indefinite under 35 U.S.C. 112, second paragraph.

Claim 12 recites a biodegradable polycation compound according to claim 1, having an amphiphilic residue, wherein said amphiphilic residue is selected from the group consisting of fatty chains, phospholipids, cholesterol, ethylene or propylene glycol oligomers, propylene glycol oligomers and combinations thereof. Claim 1 recites the additional limitation that the amphiphilic group contains an aliphatic chain of at least 4 carbons.

One of ordinary skill in the art knows the meaning of the term cholesterol derivatives. For example, the USPTO's U.S. Manual for Classification defines *cholesterols* as compounds containing the cyclopentanohydrophenanthrene ring system. The phenanthrene portion of this tetracyclic system cannot be completely aromatic; it must be hydrogenated to some degree. Included in this definition are compounds which contain an additional ring fused to one or more of the rings of the cyclopentanohydrophenanthrene ring system. The ring system is numbered, as shown in the attached printouts, in order to indicate the position of substituents. The relevant sections of the manual are enclosed.

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Hydrophobic and/or amphiphilic groups attached to the polymer backbone have the capacity to allow penetration of the complex into the cell (page 13, lines 6-10). The references enclosed with the response filed on January 21, 2004 illustrate a number of cholesterol derivatives which allow penetration into the cell for the purposes of gene transfer.

As evidenced by the printouts submitted with this response, one of ordinary skill in the art would understand, in view of the applicant's disclosure, that the term cholesterol refers to cholesterol which has been chemically modified (i.e. derivatives) to allow penetration of the complex into the cell for purposes such as gene transfer (transfection). The scope of claim 12 is clear. Therefore, claim 12 is not indefinite under 35 U.S.C. 112, second paragraph.

Claim 25 recites a biodegradable composition, according to claim 2, in combination with cationic and nonionic lipids or polymers for enhanced cell transfection.

As discussed above, definiteness of claim language must be analyzed, not in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary skill in the pertinent art at the time the invention was made.

One of ordinary skill in the art knows the meaning of the terms cationic and nonionic lipids or polymers. For example, the article entitled "The Use of Synthetic

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Polymers for the Delivery of DNA", a copy of which is enclosed, describes the use of cationic lipids and cationic polymers for gene delivery.

The addition of an anionic, cationic or amphilic polymers or lipids to a plasmd: DNA complex can significantly enhance the transfection efficiency of the complex. Suitable polymers, oils, surfactants, and lipids are described on page 11, lines 2-8; page 19, lines 1-3; page 19, lines 20-28; and page 20, line 30 to page 21, line 12.

As evidenced by the printouts submitted with this response, one of ordinary skill in the art would understand, in view of the applicant's disclosure, that the terms polymers and lipids refers to cationic and nonionic polymers and lipids which are able to interact with the polysaccharide-anionic macromolecule complex and as a result enhance the degree and efficiency of transfection.

**Double Patenting Rejection**

Claims 1-26 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Application Serial No. 10/031,728. In response, Applicants submit a terminal disclaimer to overcome the double patenting rejection.


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Allowance of claims 1-26, as amended, is respectfully solicited.

Respectfully submitted,



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